REMARKS

Claims 1-19, 21-23, and 26-29 are pending. By this Amendment, no claims are cancelled, independent claim 27 is amended, and no new claims are added. Support for this Amendment can be found in the specification as originally filed, and no new matter is believed to be introduced.

Claim Rejections – 35 U.S.C. § 103

The December 17, 2010 Office Action rejected claims 1, 3-19, 21-23 and 26-29 under 35 U.S.C. § 103(a) as being unpatentable over Cross et al. (Nature Genetics, Vol. 6, No. 3, pp. 236-244 (1994)) in view of Wiemann (WO 2001/12659). Applicants respectfully traverse the rejection as a *prima facie* case of obviousness has not been established.

Independent Claim 1

Independent claim 1 of the presently claimed invention is directed to a method of separating and/or enriching prokaryotic DNA, comprising the steps of (a) contacting at least one prokaryotic DNA, present in solution, with a protein which specifically binds prokaryotic DNA and has 25% to 35% homology with the wild type CGBP protein, thereby forming a protein-DNA complex, and (b) separating said complex. In the presently claimed method, the protein specifically binds prokaryotic DNA.

In stark contrast, Cross et al. discloses an affinity column that utilizes a protein fragment (MDB) to fractionate genomic human DNA according to the level of CpG motif methylation ***of the same DNA fragment***. (*See* page 236, Col. 2, ¶ 2 under the sub-title "Fractionation of DNA using an MDB column".) Essentially, Cross et al. describes a fractionation method for genomic

human DNA according to different methylation conditions, wherein a large quantity (100 μg) of genomic DNA is used as the starting material. (*See* page 243, right column, first sentence under "Preparation of the CpG island fraction"; *and Cf.* with page 236, left column, lines 1-6 which corresponds to 98 μg methylated and 2 μg non-methylated DNA.) In other words, Cross et al. teaches a protein binding to methylated and non-methylated ***eukaryotic*** DNA. Cross et al. fails to teach, disclose or suggest the claim limitation of a protein binding to ***prokaryotic*** DNA, much less the protein as presently claimed in independent claim 1.

Thus, a *prima facie* case of obviousness has not been established, as the cited references, individually or in combination, do not teach or suggest all of the features included in independent claim 1. If an independent claim is non-obvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837, F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, Applicants are not presenting additional arguments with respect to the patentability of the dependent claims, although Applicants do not acquiesce to any of the rejections and reserve the right to raise additional arguments with respect to the patentability of such claims. As all remaining pending claims depend directly or indirectly from one of the subject claims, Applicants respectfully request that the rejections under § 103 be withdrawn. Also, because a *prima facie* case of obviousness has not been established, Applicants do not comment further here on the suitability of combining or modifying the cited references. Thus, Applicants respectfully request reconsideration and withdrawal of these rejections.

Independent Claim 27

Independent claim 27 of the presently claimed invention as amended is directed to a method of separating and/or enriching non-methylated DNA from a mixture of non-methylated

and methylated DNA by providing a mixture containing at least one non-methylated DNA and at least one methylated DNA, contacting the mixture in a solution with a protein having between about 25% and 35% homology with a wild type CGBP protein to specifically bind the protein and the at least one non-methylated DNA, thereby forming a protein-DNA complex, and separating the complex, such that the protein does not specifically bind to the at least one methylated DNA.

In stark contrast, Cross et al. describes the binding affinity on the affinity column to fractionate genomic human DNA according to the level of CpG motif methylation of the same DNA fragment as depending on the methyl-CpG density. Specifically, Cross et al. discloses "[t]he tight binding of multiple methylated DNA molecules presumably involves interaction of one DNA molecule with several different MBD moieties." (*See* page 237, first full paragraph on left column.) Cross et al. also teaches the protein fragment has a specific DNA-binding activity to methylated DNA and a weak non-specific DNA-binding activity to non-methylated DNA. (*See id.*) In other words, Cross et al. teaches that the protein fragment binds to both methylated and non-methylated DNA. Cross et al. fails to teach, disclose or suggest the claim limitation of a protein specifically binding to non-methylated DNA to form a protein-DNA complex while not specifically binding to the methylated DNA, much less the protein as presently claimed in independent claim 27.

Thus, a *prima facie* case of obviousness has not been established, as the cited references, individually or in combination, do not teach or suggest all of the features included in independent claim 27 as amended. If an independent claim is non-obvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837, F.2d 1071, 5 USPQ2d 1596 (Fed.

Cir. 1988). Therefore, Applicants are not presenting additional arguments with respect to the patentability of the dependent claims, although Applicants do not acquiesce to any of the rejections and reserve the right to raise additional arguments with respect to the patentability of such claims. As all remaining pending claims depend directly or indirectly from one of the subject claims, Applicants respectfully request that the rejections under § 103 be withdrawn. Also, because a *prima facie* case of obviousness has not been established, Applicants do not comment further here on the suitability of combining or modifying the cited references. Thus, Applicants respectfully request reconsideration and withdrawal of these rejections.

Additional comments regarding cited references

Morever, "[i]n determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." MPEP 2141.02 (V) (emphasis in original) (*citing Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983)); *Schenk v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). Also, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." MPEP 2141.03 (VI) (emphasis in original) (*citing W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 202 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)). Further, "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. MPEP 2143.02(VI) (*citing In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)).

When properly considered in its entirety (i.e., as a whole), Cross et al. teaches away from the presently claimed invention. Cross et al. is directed to fractionalization of genomic human DNA according to the level of CpG motif methylation of the same eukaryotic DNA fragment, as opposed to a protein having specific binding to prokaryotic DNA (claim 1). Cross et al. also teaches that the protein fragment specifically binds to methylated DNA and has non-specific binding to non-methylated DNA, as opposed to a protein that specifically binds to non-methylated DNA (claim 27).

Also, there is no reasonable basis to conclude that one of ordinary skill in the art would modify or combine Cross et al. to read on the presently claimed invention. Any such modification or combination would change the principle of operation of Cross et al. The basis principle under which the method of Cross et al. operates is a protein that **specifically binds to methylated DNA** and has a **weak non-specific DNA-binding activity to non-methylated DNA** in order to fractionate **eukaryotic** DNA based upon the level of methylation.

Further, Wiemann uses the CpGP-protein for an entirely different method, as it appears to deal with providing of certain sequences in analytic scale by interpreting the obtained expression patterns. It appears that only one single target of the disclosed gene expression pattern is the CpGP protein. This is an entirely different approach than the presently claimed invention. Given the inherent uncertainty within the chemical arts, there is no reasonable basis that the use of the CpGP-protein of Wiemann in the Cross et al. method would have a reasonable expectation of success, much less any degree of predictability.

Thus, a *prima facie* case of obviousness has not been established, as the cited references, individually or in combination, are not suitably modified or combined to teach or suggest the

currently claimed invention. If an independent claim is non-obvious under 35 U.S.C. 103, then any claim depending therefrom is non-obvious. *In re Fine*, 837, F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, Applicants are not presenting additional arguments with respect to the patentability of the dependent claims, although Applicants do not acquiesce to any of the rejections and reserve the right to raise additional arguments with respect to the patentability of such claims. As all remaining pending claims depend directly or indirectly from one of the subject claims, Applicants respectfully request that the rejections under § 103 be withdrawn. Also, because a *prima facie* case of obviousness has not been established, Applicants do not comment further here on the suitability of combining or modifying the cited references. Thus, Applicants respectfully request reconsideration and withdrawal of these rejections.

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

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